UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,950	10/08/2003	Robert W. Langley	96-03	6033

23713 7590 01/18/2008

GREENLEE WINNER AND SULLIVAN P C
4875 PEARL EAST CIRCLE
SUITE 200
BOULDER, CO 80301

EXAMINER	
DEAK, LESLIE R	
ART UNIT	**PAPER NUMBER**
3761	

MAIL DATE	DELIVERY MODE
01/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/680,950	LANGLEY ET AL.	
	Examiner	Art Unit	
	Leslie R. Deak	3761	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53 and 56-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-53 and 56-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-12, 14-15, 17-40, 42-45, 47-50, 67 arerejected under 35 U.S.C. 103(a) as being unpatentable over US 6,179,801 to Holmes et al in view of US 5,980,465 to Elgas.

In the specification and figures, Homes discloses the method substantially as claimed by Applicant. With regard to claims 25-27, Holmes discloses a blood processing apparatus and method that comprises the steps of entering patient data into a control screen to calculate the donor's total blood volume and using the total blood volume in the determination of various parameters of the apheresis procedure (see column 56, lines 61 to column 57, line 2). Holmes specifically discloses that blood inlet pump 1030 is operated according to parameters stored in blood component separation device 6, which receives the patient parameters described above (see column 27, lines 15-25). Therefore, the removal of blood from the patient via removal pump 1030 is performed in a manner derived from the predetermined operating protocol stored in apheresis machine 6, which operates, in part, on patient blood volume data. Similarly, Homes discloses that the return rate of the blood return submode via return pump 1090 is

established by blood component separation device 6 according to a predetermined protocol (see column 27, lines 15-25).

Holmes fails to disclose the step of adjusting a removal and/or flow rate during the blood processing procedure based on the total blood volume. However, Elgas discloses a method for detecting changes in patient's blood volume during extracorporeal treatments. Elgas discloses that maintaining a patient's total blood volume during extracorporeal procedures is clinically significant to maintaining physiological status, teaches that increasing fluid flow to the patient in the event of total blood volume decrease is a good way to maintain that status quo (see column 1, lines 31-57). Such a disclosure reasonably suggests to one of ordinary skill in the art other steps, such as adjusting blood withdrawal rate, would be within the range of reasonable steps taken to maintain the patient's total blood volume. It would have been obvious to one having ordinary skill in the art at the time of invention to use the suggestion of the Elgas disclosure with regard to maintaining patient total blood volume through fluid flow rate adjustments in the apheresis procedure disclosed by Holmes in order to maintain physiological status quo of the patient, as taught by Elgas. Accordingly, the combination of the Holmes and Elgas references suggest the method claimed by Applicant.

With regard to Applicant's claims drawn to "systematic" variance of flow rates (eg, claims 1, 23), Holmes clearly discloses that the apheresis system 6 varies the flow rates based on a predetermined operating scheme (see column 27, lines 15-25, column 56, lines 60-67). Since the system controls such variations, Examiner considers flow rates adjusted by the apheresis system 6, including elimination of flow at the end of the

processing period (see column 28, lines 40-44) to correspond to Applicant's "systematic" variations, since the variations are derived from the system

With regard to claims 12, 40, and 67, Holmes specifically discloses that blood is removed and returned through patient access 30 and needle 32 (see FIG 2A).

With regard to claims 42, 43, 21, and 22, Holmes discloses that the blood processing method includes a blood removal submode and a blood return submode that repeat sequentially for a predetermined amount of time (see column 28, lines 40-44).

With regard to claims 44, 45, 14, and 15, Holmes specifically discloses that the blood processing procedure may be used to separate a patient's whole blood via a centrifuge into constituent components, wherein one or more components are retained by the system (corresponding to Applicant's claimed collect component) and the undesired components are returned to the patient (see column 1, lines 16-25; see also column 8, lines 20-60 for density centrifuge).

With regard to claims 47-50 and 17-20, Holmes discloses that the collected component may comprise red blood cells, white blood cells, platelets, or plasma (see column 1, lines 16-25)..

With regard to claim 1, Holmes discloses that the return pump 1090 may be started and stopped according to the operating parameters of the system, thereby varying the rate of fluid return to the patient (see column 27, lines 25-35).

With regard to claim 2, Holmes discloses that the return pump 1090 is stopped after the completion of the return time (see, for example, column 28, lines 40-43). Such

a stoppage represents a decrease in the return flow rate, thereby meeting the limitations of the claim.

With regard to claim 11, Holmes discloses that the blood removal submode may be stopped in response to signals from the blood separation device 6, thereby halting blood removal pump 1030 (see column 27, lines 10-15). Such stopping of the blood pump is considered by the examiner to vary the rate of the removal, meeting the limitations of the claim.

With regard to claims 3, 8, 9, and 10, Holmes specifically discloses in column 56, lines 61-67, that patient data such as patient blood volume are used to establish the operating parameters of the apheresis device 6, thereby regulating the disclosed blood processing method. In column 27, lines 15-25, Holmes teaches that the volume transfer rate of blood flow is variable based on a "predetermined protocol" of the apheresis machine 6. Accordingly, this flow rate is regarded as a result-effective variable (see also at least column 28, lines 44-67 for discussion of variable flow rates). It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, Examiner considers the flow rates claimed by Applicant (eg, increasing, decreasing, exponentially decreasing, or linearly varying) to be a result-effective variable (the adjustment of which does not patentably distinguish over the prior art of record) that may be controlled by collected and calculated patient data, thereby meeting the limitations of the claims.

With regard to claims 4-7, 30-31, and 34-39, Applicant claims to establish a return flow rate based on a specific equation. As noted above, Holmes discloses that

the flow rate is recognized to be a result-effective variable. These claims establish a method for setting/optimizing various flow rates via the selection of variable/optimal parameters. Absent a disclosure that Applicant's claimed equations provide a significant advantage over the prior art's calculation, Examiner considers the selection of such variable parameters to be mere optimization of a result-effective variable through routine experimentation. Holmes specifically teaches that such parameters may be selected as desired by the operator and blood handling procedure (see, generally, columns 27-28). Accordingly, as previously noted, the optimization of a variable flow rate is not considered to patentably distinguish Applicant's invention from the prior art of record. See MPEP 2144.05.

With regard to claim 23, Holmes discloses that the blood removal submode may be stopped in response to signals from the blood separation device 6, thereby halting blood removal pump 1030 (see column 27, lines 10-15). Such stopping of the blood pump is considered by the examiner to vary the rate of the removal, meeting the limitations of the claims. With regard to Applicant's claim limitation drawn to the ability of the method to reduce vessel infiltration, Applicant discloses that such infiltration is generally a result of large pressure fluctuations while withdrawing or returning fluid to the patient's blood vessel. Holmes specifically discloses that pressure sensor 1200 senses negative and positive pressure changes in the removal tubing 22 and return tubing 26. The pressure signals are conveyed to the separation device 6, which controls the operation of removal pump 1030 and return pump 1090 (and thereby the flow rate) to maintain predetermined fluid pressures during the procedure (see column 27, lines

36-61). Holmes discloses that the pressure is controlled, which necessarily controls what Applicant discloses is the cause of infiltration. It follows naturally that in controlling the pressure, the rate of infiltration is also controlled, thereby meeting the limitations of the claim.

With regard to claim 24, while increasing the removal flow rate is regarded as an optimization of a result-effective variable found in the prior art (see rejection above), Holmes specifically discloses that the blood processing method includes a blood removal submode and a blood return submode that repeat sequentially for a predetermined amount of time (see column 28, lines 40-44).

With regard to claims 28 and 29, as previously noted, Holmes uses the total blood volume of the patient in the determination of various parameters of the apheresis procedure (see column 56, lines 61-67). Furthermore, Holmes appears to suggest that such parameters include the withdrawal and return flow rates (see, generally, columns 27-28). Therefore, the linear correlation of the flow rate and increase of the flow rate found in the claims would be a matter of optimizing a result-effective variable found in the prior art. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, Examiner considers the flow rates claimed by Applicant (eg, increasing, decreasing, exponentially decreasing, or linearly varying) to be a result-effective variable (the adjustment of which does not patentably distinguish over the prior art of record) that may be controlled by collected and calculated patient data, thereby meeting the limitations of the claims.

With regard to claims 32 and 33, Applicant attempts to claim a method for determining blood volume with a formula based on patient sex, height, and weight. Holmes discloses that his procedure comprises a method for determining blood volume based on patient sex, height, and weight (see column 56, lines 48-67). Without a disclosure of how Applicant's formula improves the determination of blood volume from that found in the prior art, Examiner considers the claimed formula to be merely a matter of optimizing the manner in which each procedure arrives at the patient's total blood volume. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, Examiner considers Applicant's selection of variable coefficients in an equation to be a matter of routine experimentation that optimizes accurate determination of patient blood volume.

3. Claims 13, 16, 41, 46, 51-53, and 56-66, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,179,801 to Holmes et al in view of US 5,980,465 to Elgas, further in view of US 6,730,054 to Pierce et al.

In the specification and figures, Holmes and Elgas suggest the method substantially as claimed by Applicant (see rejection above) with the exception of two needles to draw and return blood, an elutriation centrifugation, and a recirculation step.

With regard to claims 13 and 41, Pierce discloses a blood processing system that draws blood from a patient based on patient parameters such as patient blood volume, separates the blood into components, and returns the unused component to the patient (see column 1, lines 50-55, column 3, lines 57-63, column 12, lines 54-61). Pierce

discloses that the system may comprise either a single needle blood collection system or a double needle system (see column 2, lines 65-67). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to perform the blood processing procedure suggested by Holmes and Elgas with a two needles as disclosed by Pierce, since Pierce teaches that single and double needle processing systems are interchangeable.

With regard to claims 51 and 53, Pierce discloses a recirculation procedure that adds separated PRP to entering whole blood in order to maximize the separation of RBC and PRP to prevent contamination with RBC (see column 8, lines 54-65). As such, Pierce discloses the steps of conducting removed, anticoagulated WB through system 10, wherein the system collects RBC and PRP (see column 8, lines 29-32). The system collects a portion of the PRP for further processing (corresponding to Applicant's first portion), and recirculates a portion of the PRP through the system to combine with WB for increased separation efficiency (wherein the recirculated PRP corresponds to Applicant's claimed second portion) (see column 8, lines 29-60). During this mode, the controller returns unused RBC and PPP (corresponding to Applicant's third component) to the patient. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to add a recirculation step as disclosed by Pierce to the blood separation and collection procedure as suggested by Holmes and Elgas, in order to provide maximal separation of RBC and PRP, as taught be Pierce.

With regard to claims 16, 46, and 56, Pierce's recirculation of PRP into the collected WB creates a secondary elutriation process that increases the separation of

platelets from WB by adding extra PRP as a washing fluid to provide maximal separation of RBC and PRP. Accordingly, Pierce discloses a blood separation procedure that uses both density centrifugation and elutriation to separate the desired blood components, meeting the limitations of the claims. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use a washing/elutriation process as disclosed by Pierce in the blood processing procedure suggested by Holmes and Elgas, in order to increase separation efficiency, as taught be Pierce.

With regard to claim 52, Holmes discloses that the blood processing method includes a blood removal submode and a blood return submode that repeat sequentially for a predetermined amount of time (see column 28, lines 40-44).

With regard to claims 63-66, Holmes discloses that the collected component may comprise red blood cells, white blood cells, platelets, or plasma (see column 1, lines 16-25).

With regard to claims 57 and 58, the prior art discloses both a removed blood portion and a recirculated blood portion, each of which necessarily has a hematocrit value. This weighted average of the hematocrit values necessarily varies with the amount of blood supplied to the processing device. Pierce teaches that hematocrit values are calculated based on flow considerations (see column 7, lines 14-20). Accordingly, variation of flow conditions necessarily varies hematocrit values, creating a result-effective variable. As understood in the art, hematocrit values of separated portions may vary with variations in flow conditions that alter the efficiency of

separation, which may result in higher or lower hematocrit concentration in a recirculated portion. Since hematocrit value is based on flow conditions, the flow conditions may be manipulated in to create the hematocrit ratio claimed by applicant.

Pierce does not provide any limitation to the amount of fluid supplied to the withdrawn blood in the recirculation loop, but does disclose that the amount is sufficient to establish desired conditions in the blood separation system. Therefore, Pierce suggests that the amount of recirculated portion combined with the removed blood may be selected to maximize a desired result—efficient separation of RBC and PRP. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, the portion of the recirculated flow is selected to provide the result of maximum separation of RBC and PRP.

With regard to claims 59-62 and 68, as noted above, each portion of blood necessarily has a hematocrit value, and the draw and return cycles each have a rate (see rejections above). Applicant uses an equation to set the duration of each cycle. Both Holmes and Pierce teach that the method comprises draw and return cycles. Broadly defined, a cycle comprises an interval of time (see Merriam-Webster's Collegiate Dictionary, 10th Ed., 2001). All the values used in the determination of $F_{c\,max}$ in the claimed equation are demonstrated by the prior art to be variable. It has been held that the optimization of a result-effective variable involves only routine skill in the art. See MPEP 2144.05. In the instant case, the duration of the draw and return cycles are varied in order to provide a sufficient amount of time to provide blood to the separation system and to return components to the donor, respectively. (see Pierce,

column 7, lines 45-50). Accordingly, Examiner considers the selection of such variable parameters to be mere optimization of a result-effective variable through routine experimentation.

Response to Arguments

4. Applicant's arguments filed 14 November 2007 have been entered and fully considered. However, Applicant's arguments are not persuasive.

5. Applicant argues that Holmes does not disclose adjusting the blood removal rate or return rate based on the patient's total blood volume. Examiner agrees and has rejected the instant claims over Holmes in view of Elgas, as set forth above.

6. Applicant argues that Elgas does not teach adjustment of patient blood volume by increasing or decreasing blood removal or return rates, but rather by separate administration of another fluid. However, Examiner notes that Elgas specifically teaches that the circulatory fluid of the patient (consisting of blood and IV fluids) is removed from the vena cave via a *variable speed roller pump*, indicating that the Elgas device is capable of varying fluid removal rate from the patient (see column 2, lines 40-48). Nonetheless, the Examiner is not relying on the Elgas reference to teach the variation of blood removal and/or return rates. Holmes clearly teaches that blood removal and/or return rate may be adjusted throughout the procedure according to patient parameters (see at least column 27). Holmes does not disclose that the patient parameters may include total blood volume of the patient. Elgas teaches that total blood volume of the patient may be monitored as a particular patient parameter in order to adjust an

extracorporeal procedure according to patient parameters. The Examiner is not relying on the Elgas reference to teach adjustment of fluid removal and return rates based on patient blood volume, but merely to illustrate that patient blood volume is one of the many patient parameters that may be used to control an extracorporeal procedure as disclosed by Holmes, in order to maintain patient comfort.

7. Applicant argues that total blood volume has not been recognized as a result-effective variable which achieves a recognized result. Examiner respectfully disagrees. Elgas suggests that adjustment of total patient fluid volume may be accomplished via IV infusion, but also discloses a variable speed pump that removed fluid from the patient, suggesting that fluid removal rate may also be used to control patient fluid volume. Taken together, the references reasonably suggest that manipulation of fluid removal and/or return rates are variables, that when manipulated, control total patient fluid volume. Accordingly, the references suggest that variation of the fluid removal and return rates are result-effective variables that may be controlled by collected and calculated patient data, thereby meeting the limitations of the claims.

8. Applicant further argues that the specification provides results that the claimed methods demonstrate improvement in performance over the prior art. However, Applicant's claimed results are not backed up by sufficient experimental data. It is well settled that unexpected results must be established by factual evidence. See MPEP 716.01(c). Due to the absence of detailed experimental data comparing Applicant's invention with the closest prior art, it is the position of the Examiner that Applicant's assertions of decreased vein infiltration constitute mere argument.

Furthermore, Applicant does not establish that the decreased incidence of vein infiltration disclosed in the specification constitutes unexpected results. Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. See MPEP 716.02. Accordingly, it is the position of the Examiner that the results disclosed by Applicant are not unexpected, and are therefore insufficient to overcome a *prima facie* case of obviousness.

9. Applicant argues that the Pierce reference fails to overcome the deficiencies of Holmes and Elgas. Examiner respectfully disagrees. Holmes and Elgas suggest the method as claimed by Applicant. With regard to claims 57-58, Applicant merely claims that a first portion of fluid and a second portion of fluid comprise a particular hematocrit ratio, but does not disclose or claim what steps are taken in the method to establish such a ratio. Pierce teaches that hematocrit values are calculated based on flow considerations (see column 7, lines 14-20). Accordingly, variation of flow conditions necessarily varies hematocrit values, creating a result-effective variable. As understood in the art, hematocrit values of separated portions may vary with variations in flow conditions that alter the efficiency of separation, which may result in higher or lower hematocrit concentration in a recirculated portion. Since hematocrit value is based on flow conditions, the flow conditions may be manipulated in to create the hematocrit ratio claimed by applicant. Examiner is not asserting that hematocrit ratios are used to control the efficacy of the blood separation device, but that the variation of flow rates and combination of recirculated fluid with removed blood, as disclosed by Pierce,

amounts to a manipulation of a result-effective variable (flow rate), wherein the efficiency of separation comprises the result. Such manipulation may arrive at the hematocrit ratios claimed by applicant, suggesting the limitations of the claims.

With regard to claims 59-62 and 68, Pierce discloses that hematocrit values are affected by flow conditions, which include the duration of the draw and return cycles. Since the duration of the draw cycle affects the length of time the withdrawn blood is processed, it necessarily affects the hematocrit value of both the collected portion and the recirculated portion. The duration of the return cycle affects the amount of fluid and the frequency at which the fluid is returned to the patient, affecting the hematocrit of the whole blood. Accordingly, the duration of the draw and return cycles necessarily affects the hematocrit values, and therefore the ratio between the hematocrit of the whole blood, collected portion, and the recirculated portion. Accordingly, the manipulation of the duration of the draw and return cycles amounts the manipulation of a result-effective variable (the duration of each cycle), wherein the efficiency of separation comprises the result.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie R. Deak whose telephone number is 571-272-4943. The examiner can normally be reached on Monday - Friday, 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tanya Zalukaeva can be reached on 571-272-1115. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leslie R. Deak
Patent Examiner
Art Unit 3761
7 January 2008